CLAIMS

1. Method of analysis of the toxic potential of a test compound, comprising at least one hybridization step between a) a nucleic acid sample from cells treated with this compound and b) a nucleic acid bank corresponding to genetic events characteristic of deregulation(s) in cell signalling pathway(s), the hybridization profile indicating the toxic potential of the test compound.

2. Method of analysis of the toxic potential of a test compound, comprising at least a separate hybridization step between a) labelled nucleic acid probes corresponding to RNA from untreated cells and cells treated with said test compound and b) a nucleic acid bank corresponding to genetic events (transcriptional and/or splicing events) characteristic of a situation(s) of deregulation in cell signalling pathway(s), the hybridization profile indicating the toxic potential of the test compound.

3. Method according to claim 1 or 2, characterized in that the nucleic probes a) correspond to messenger RNA from treated and untreated cells.

4. Method according to one of claims 1 to 3, characterized in that the nucleic probes a) are cDNA or cDNA fragments prepared from the RNA of treated and untreated cells.

5. Method according to any one of the previous claims, characterized in that the nucleic probes a) are amplification products.

6. Method according to any one of the previous claims, characterized in that the nucleic probes a) are labelled by radioactive, fluorescent, enzymatic or colorimetric labels.

7. Method according to any one of the previous claims, characterized in that the test compound is an individual compound or is present in a mixture with other substances.

8. Method according to any one of the previous claims, characterized in that the bank b) comprises nucleic acids corresponding to genes whose level of expression is modified in situations of deregulation(s) of cell signalling pathway(s).

9. Method according to one of claims 1 to 7, characterized in that the bank b) comprises nucleic acids of which at least part of the sequence corresponds to the sequence of genes that are differentially spliced during deregulation(s) of cell signalling pathway(s).

10. Method according to one of claims 1 or 2, characterized in that the bank b) comprises nucleic acids according to claim 8 and nucleic acids according to claim 9.

11. Method according to claim 9, characterized in that the bank b) is prepared by hybridization between a nucleic acid population from a cell in a situation of deregulation(s) of cell signalling pathway(s), and a nucleic acid population from a cell in a control situation, and separating, from the hybrids formed, nucleic acids corresponding to differential splicings.

12. Method according to any one of the previous claims, characterized in that the situation of deregulation is induced by modification of the activation, preferably of the expression of a gene that initiates or carries out apoptosis.

13. Method according to claim 12, characterized in that the situation of deregulation is produced by induction or enhancement of the activation, preferably of the expression of an anti-oncogene.

14. Method according to claim 13, characterized in that the anti-oncogene is chosen from among p53, Rb, p73, myc, TUPRO-2 and NHTS.

15. Method according to claim 12, characterized in that the situation of deregulation is induced by modification of the activation, preferably of the expression of a gene involved in cell growth or viability.

16. Method according to claim 12, characterized in that the situation of deregulation is induced by constitutive or inducible activation, preferably expression of all or part of a gene involved in cell growth, cell viability or apoptosis.

17. Method according to any one of claims 1 to 7, wherein the bank b) comprises at least 1 clone of sequence selected from SEQ ID Nos: 1 to 37, more preferably at least 5.

18. Method according to any one of claims 1 to 7, wherein the bank b) comprises a set of probes, in particular 5 probes or more, preferably 10 probes or more, each of said probes being complementary to a part of a gene selected from the following genes : Aldolase A; S4 subunit of proteasome 26S ; Alpha-tubulin ; Glucosidase II ; lamin B receptor homologue; EF1-alpha ; Fra-1 ; tyrosine kinase AX1 receptor ; spliceosomale Protein SAP62 ; TRAF-3 ; EF2 ; TEF-5 ; CDC25b ; interleukine-1 receptor-associated kinase (« IRAK ») ; WAF-1 ; c-fos (exon 4) ; ckshs1 ; PL16 ; NFAR-2 ; phosphatidylinositol4-kinase, ERF, Eph type receptor tyrosine kinase (hEphB1b) ; BAF60b protein of the SWI/SNF complex ; EB1 ; MSS1 ; retinoïc acid alpha receptor (RARa) ; translation initiation factor eiF4A ; STE20 type

kinase ; protein HSP 90kda ; Lipocortin II ; protein TPT1 (« translationally controlled tumor proteon »); Hsc70 ; Cytokeratin 18 ; 2-oxoglutarate dehydrogenase ; mitochondrial gene NADH6 ; mitochondrial gene NADH deshydrogenase 4 ; alpha subunit of mitochondrial ATP synthase.

19. Method according to any one of the previous claims, characterized in that the treated or untreated cells a) and the cells in a situation of deregulation b) are of a different type.

20. Method according to any one of the previous claims, characterized in that the treated or untreated cells are mammalian cells, preferably of human origin.

21. Method according to any one of the previous claims, characterized in that the treated or untreated cells are cell lines.

22. Method according to any one of the previous claims, characterized in that the treated or untreated cells are primary cultures.

23. Method according to any one of the previous claims, characterized in that the treated or untreated cells are cells extracted from the organs or tissues of treated or untreated animals.

24. Method of diagnosis of the toxic potential of a test compound, comprising at least the hybridization between, on the one hand, labelled nucleic probes corresponding to mRNA from untreated cells and a nucleic acid bank corresponding to genetic events characteristic of situation(s) of deregulation of cell signalling pathway(s) and, on the other hand, labelled nucleic probes corresponding to mRNA from cells treated with said test compound and said nucleic acid bank corresponding to genetic events characteristic of situation(s) of deregulation of cell signalling pathway(s).

25. Method according to claim 24, characterized in that the situation or situations of deregulation are situations of deregulation of cell growth and/or cell viability.

26. Method according to claim 25, characterized in that the nucleic acid bank characteristic of situation(s) of deregulation is a nucleic acid bank characteristic of cells in situations of deregulation of cell growth, notably transformed cells, in particular tumor cells.

27. Method according to claim 24, characterized in that the nucleic acid bank comprises at least 1 clone of sequence selected from SEQ ID Nos: 1 to 37, more preferably at least 5.

28. Use of nucleic acid clones corresponding to genetic events (transcriptional and/or splicing events) characteristic of situation(s) of deregulation of cell signalling pathway(s), as genetic markers of toxicity.

29. Use according to claim 28, of a clone of sequence selected from SEQ ID Nos: 1 to 37.

30. Kit for the study of the toxic potential of a test compound, comprising at least :

- a nucleic acid bank corresponding to genetic events (transcriptional and/or splicing events) characteristic of situation(s) of deregulation of cell signalling pathway(s)

31. Kit according to claim 30, characterized in that the bank is a nucleic acid bank characteristic of cells in situations of deregulation of cell growth or cell viability.

32. Kit according to claim 30, wherein the bank comprises at least 1 clone of sequence selected from SEQ ID Nos: 1 to 37, more preferably at least 5.

33. Kit according to any one of claims 30 to 32, wherein the bank is deposited on a support.

34. Nucleic acid bank comprising nucleic acid clones corresponding to genetic events (transcriptional and/or splicing events) common to cells in a situation(s) of deregulation of cell signalling pathway(s) and a toxic situation.

35. Bank according to claim 34, wherein the bank comprises at least 1 clone of sequence selected from SEQ ID Nos: 1 to 37, more preferably at least 5.

36. Process of production of genetic markers of toxicity, comprising hybridization between a nucleic acid population derived from cells in a situation(s) of deregulation of cell signalling pathway(s), and a nucleic acid population derived from cells in a control situation, the isolation from the hybridization product of clones characteristic of the situation(s) of deregulation of cell signalling pathway(s), and the hybridization of the clones obtained with a nucleic acid sample derived from cells in a situation of toxicity.

37. Process of preparation of a DNA chip that can be used to diagnose the potential toxicity of a test compound, comprising the application on a solid support of one or more nucleic acid preparations characteristic of situation(s) of deregulation of cell signalling pathway(s).

38. A method for the identification of SNPs or other mutations or polymorphisms that allow the assessment of the response of a subject to a given compound, the method comprising (i) the identification in vitro of nucleic

acids characteristic of splicing events induced in a cell treated with said compound and (ii) the identification of SNPs or other mutations or polymorphisms in the gene or genes corresponding to nucleic acids identified in (i), said SNPs or other mutations or polymorphisms allowing the assessment of the response of a subject to said given compound.

39. A method for the evaluation of the sensitivity or of the response of a subject to a test compound, comprising the analysis, from a biological sample comprising DNA from said subject, of the presence in the DNA of said subject of polymorphisms, SNPs, or other genomic alterations present in genes whose splicing is modified in response to said compound.